

IN THE CLAIMS

Please amend claims 16, 17, 22, 23, 33 and 34 and add new claim 36 as follows:

1-14. (WITHDRAWN)

15. (CANCELLED)

16. (CURRENTLY AMENDED) The method of claim 33, wherein the ~~first insulin species is human insulin and the second insulin species is AspB28 insulin a variant of human insulin having at least one amino acid substitution.~~

17. (CURRENTLY AMENDED) The method of claim 33, wherein the second insulin species is LISPRO insulin ~~variant of human insulin is LISPRO insulin.~~

18. (ORIGINAL) The method of claim 17, wherein the human insulin comprises from about 1% to about 50% of the insulin of the composition and wherein the LISPRO insulin comprises from about 50% to about 99% of the insulin of the composition.

19. (PREVIOUSLY PRESENTED) The method of claim 18, wherein the human insulin comprises from about 5% to about 20% of the insulin of the composition and wherein the LISPRO insulin comprises from about 95% to about 80% of the insulin of the composition.

20. (PREVIOUSLY PRESENTED) The method of claim 33, wherein the composition is a pharmaceutical composition.

21. (CANCELLED)

22. (CURRENTLY AMENDED) The method of claim 34, wherein the ~~first insulin species is human insulin and the second insulin species is AspB28 insulin a variant of human insulin having at least one amino acid substitution.~~

23. (CURRENTLY AMENDED) The method of claim ~~23~~ 34, wherein the ~~variant of human insulin~~ second insulin species is LISPRO insulin.

24. (ORIGINAL) The method of claim 23, wherein the human insulin comprises from about 1% to about 50% of the insulin of the composition and wherein the LISPRO insulin comprises from about 50% to about 99% of the insulin of the composition.

25. (ORIGINAL) The method of claim 24, wherein the human insulin comprises from about 5% to about 20% of the insulin of the composition and wherein the LISPRO insulin comprises from about 95% to about 80% of the insulin of the composition.

26. (ORIGINAL) The method of claim 25, wherein the composition is a pharmaceutical composition.

27-32. (WITHDRAWN)

33. (CURRENTLY AMENDED) A method of making an insulin heterodimer composition, the method comprising:

(a) selecting a first insulin species comprising human insulin and a second insulin species comprising a human insulin polypeptide having an amino acid substitution at position 28 in the beta chain;

(b) adding the first insulin species and the second insulin species together in a aqueous solution comprising a pharmaceutically acceptable carrier;

(c) allowing the first insulin species and the second insulin species to associate in the solution so that the insulin heterodimer composition is made;

wherein the first insulin species and the second insulin species are selected so that the heterodimer formed by the first insulin species and the second insulin species is more stable than a homodimer ~~formed by the first insulin species or a homodimer formed by the second insulin species~~.

34. (CURRENTLY AMENDED) A method of stabilizing an insulin composition comprising:

(a) selecting a first insulin species comprising human insulin and a second insulin species comprising:

a human insulin polypeptide having a P28D amino acid substitution in the insulin beta chain; or

a human insulin polypeptide having a P28K/K29P amino acid substitution in the insulin beta chain;

wherein the first insulin species and the second insulin species are selected such that a heterodimer formed by the first insulin species and the second insulin species is more stable than a homodimer ~~formed by the first insulin species or a homodimer~~ formed by the second insulin species;

(b) adding the first insulin species and the second insulin species together in a aqueous solution comprising a pharmaceutically acceptable carrier;

(c) allowing the first insulin species and the second insulin species to associate in the solution so that a insulin heterodimer is formed by the first insulin species and the second insulin species; so that the insulin composition is stabilized.

35. (PREVIOUSLY PRESENTED) A method of making an insulin heterodimer composition, the method comprising:

(a) adding human insulin and LISPRO insulin together in an aqueous solution comprising a pharmaceutically acceptable carrier;

(b) allowing the human insulin and LISPRO insulin to associate in the solution so that the insulin heterodimer composition is made;

wherein the human insulin and LISPRO insulin are selected so that a heterodimer formed by the human insulin and LISPRO insulin is more stable than a homodimer formed by the human insulin or a homodimer formed by the LISPRO insulin.

36. (NEW) A method of making an insulin heterodimer composition, the method comprising:

(a) selecting a first insulin species comprising human insulin and a second insulin species comprising a variant of human insulin polypeptide having at least one amino acid substitution;

(b) adding the first insulin species and the second insulin species together in a aqueous solution comprising a pharmaceutically acceptable carrier;

(c) allowing the first insulin species and the second insulin species to associate in the solution so that the insulin heterodimer composition is made;

wherein the first insulin species and the second insulin species are selected so that the heterodimer formed by the first insulin species and the second insulin species is more stable than a homodimer formed by the second insulin species.